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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
ANDERSON, REBECCA L	

ART UNIT	PAPER NUMBER
1626	

DATE MAILED: 11/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/662,986	MENDELOVICI ET AL.	
	Examiner	Art Unit	
	Rebecca L. Anderson	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 June 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38-43 and 89* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38-43 and 89* is/are rejected.

7)☒ Claim(s) *38-43 and 89* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 39-43 and 89 are currently pending in the instant application and are objected and rejected.

Response to Amendment and Arguments

Applicant's amendment and arguments filed 28 June 2006 have been entered into the application. Applicants' arguments have been fully considered but they are not persuasive. In regards to the claim objection of claims 39-43, applicant argues that applicant has the right to restate the invention in a reasonable number of ways and has the right to cover the invention in a reasonable number of ways by presenting claim claims having different number of limitations. This argument is not persuasive as it is proper when two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, to object to the other as being a substantial duplicate. As the instant claims 39-43 and newly added claim 89 are each claiming the same thing as claim 38, specifically the crystalline sodium salt of benzisoxazole methane sulfonic acid Form II, the claims are considered duplicates as page 20 of the instant specification defines the sodium salt of benzisoxazole methane sulfonic acid Form II as having all the properties as claimed in claims 39-43 and 89 and the data recited is considered properties of the compound and are inseparable from the compound itself.

In regards to the 35 USC 112 2nd paragraph rejection of claims 38-43 applicant argues that applicant is free to be their own lexicographer and one of skill in the art would know the meaning of BOS-Na From II recited in claim 38. This argument is not

found persuasive, as while applicant is free to be their own lexicographer, claim 38 does not contain any of the physical data that particularly points out and distinctly claims the product that Applicant regards as his invention, i.e. the claim does not provide at least the 10 strongest peaks of the X-ray diffraction data. Form II is not a limiting element and does not define a difference in the sodium salt of benzisoxazole methane sulfonic acid. Form II is not a common well recognized term in the art to define anything. While BOS-Na Form II is a term defined by the inventors, the definition is found in the instant specification as the XRD, FTIR, and water content data. It is this data that distinguishes applicants' invention from the prior art and not the term BOS-Na Form II. For example, without XRD data in the claim 38, it is impossible to distinguish applicants BOS-Na Form II from any other crystalline sodium salt of benzisoxazole methane sulfonic acid of the prior art, since there is no data in the claims to distinguish applicants' crystalline salt from any other crystalline salt of the compound. In regards to claims 39-43 applicant argues that the requirement of at least 10 strongest X-ray diffraction peaks in for identifying an unknown in comparison with a known, however, claims 39 and 40 are directed to a known compound and should not be required to recite at least 10 XRD peaks. Applicant argues that claimed 41-43 have other physical properties described and should not be required to have X-ray diffraction data as IR spectroscopy has been used for investigating the propensity of materials to form polymorphs and Fourier transform IR spectroscopy is clearly the current method of choice. This argument is not found persuasive as according to Brittain, "powder X-ray diffraction is clearly the most powerful and fundamental tool for a specification of the polymorphic identity of the

analyte. Moreover, the USP general chapter on X-ray diffraction states that the identity is established if the scattering angles of the ten strongest reflections obtained for an analyte agree to within +/- 0.20 degrees with that of the reference material, and if the relative intensities of these reflections do not vary by more than 20 percent. (see Brittain in Polymorphism in Pharmaceutical Solids, p.236). Therefore, applicants' are claiming a polymorph of the sodium slat of benzisoxazole methane sufonic acid which applicant claims is a new polymorph, which would be considered unknown. Claims 39 and 40 contain 5 or less peaks of the X-ray diffraction pattern. Claims 41-43 also contain no X-ray diffraction data. Since powder X-ray diffraction is the most powerful tool for identifying an analyte, the ten strongest peaks should be included in the claim to identify the specific polymorph claimed. However, again, additional data such as the chemical name of the compound (sodium salt of benzisoxazole methane sulfonic acid), water content and FTIR spectrum data should also be included in order to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In regards to the provisional obvious type double patenting rejection of claims 38-43 over 10/288,135, it is noted that this rejection is now not a provisional rejection as 10/288,135 has become US Patent No. 7,015,330. Applicant argues that in view of the disclosure of the XRD properties in the specification, "Form II" is sufficient to demarcate the crystalline sodium salt of benzisoxazole methane sulfonic acid according to the instant claim 38 form the crystalline sodium salt of benzisoxazole methane sulfonic acid Form IV. This argument is not persuasive as claim 38 does not contain any of the physical data that particularly points out and distinctly claims the product that Applicant

regards as his invention, i.e. the claim does not provide at least the 10 strongest peaks of the X-ray diffraction data. Form II is not a limiting element and does not define a difference in the sodium salt of benzisoxazole methane sulfonic acid. Form II is not a common well recognized term in the art to define anything. While BOS-Na Form II is a term defined by the inventors, the definition is found in the instant specification as the XRD, FTIR, and water content data. It is this data that distinguishes applicants' invention from the prior art and not the term BOS-Na Form II. For example, without XRD data in the claim 38, it is impossible to distinguish applicants BOS-Na Form II from any other crystalline sodium salt of benzisoxazole methane sulfonic acid of the prior art, since there is no data in the claims to distinguish applicants' crystalline salt from any other crystalline salt of the compound. Applicant also argues that the existence of polymorphs is unpredictable and that it is not possible to predict with confidence that a particular crystalline packing arrangement is the most stable that is likely to be found and that it is difficult to attempt to predict how many solid forms of a drug are likely to be found and therefore there is no suggestion in the prior art that the crystalline sodium salt of benzisoxazole methane sulfonic acid could be modified to form the crystalline sodium salt of benzisoxazole methane sulfonic acid Form II of the instant claim 38. Again, this argument is not persuasive as While BOS-Na Form II is a term defined by the inventors, the definition is found in the instant specification as the XRD, FTIR, and water content data. It is this data that distinguishes applicants' invention from the prior art and not the term BOS-Na Form II. For example, without XRD data in the claim 38, it is impossible to distinguish applicants BOS-Na Form II from any other crystalline sodium salt of

benzisoxazole methane sulfonic acid of the prior art, since there is no data in the claims to distinguish applicants' crystalline salt from any other crystalline salt of the compound. Applicant also argues that in regards to claims 39-43, that the examiner cannot rely on In re Cofer and Ex parte Hartop and that coupled with the knowledge in the art, a person skilled in the art would not have nay motivation, suggestion or guidance to modify Form IV to arrive at the crystalline sodium salt as instantly claimed. This argument is not persuasive as one having ordinary skill in the art would find the instant claims prima facie obvious because the instant claims differ from the known product merely by forms and the physical properties innate to the forms. As it was set forth by the court in In re Cofer 148 USPQ 268 and Ex parte Hartop 139 USPQ 525, that a product which are merely different forms of known compounds, notwithstanding that some desirable results are obtained therefrom, are unpatentable. The instant specification and claims disclose a known compound of the sodium salt of benzisoxazole methane sulfonic acid in Form II, which is ***the same pure substance*** as the prior art, only *having different arrangements and/or different conformations of the molecule*. Mere difference in physical property is well known conventional variation for the same pure substance (see Brittain p. 1-2), i.e. prima facie obvious. For a known compound with defined chemical nature to be patentable for a new form, it must have a patentability basis of an advantage in terms of stability, formulation, solubility, bioavailability, ease of purification, preparation or synthesis, hydroscopicity, recovery or prevention of precipitation, etc. As applicant has not provided an advantage, the rejection is maintained.

In regards to the provisional obvious type double patenting rejection of claims 38-43 over 10/662,966, it is noted that this rejection is withdrawn as 10/662,966 has been abandoned.

In regards to the 35 USC 102 rejections of claim 38 as being anticipated by US Patent No. 4,172,896 or FR 2428033, applicant argues that both the '896 patent and FR 2,428,033 disclose the preparation of crude crystalline sodium salt of benzisoxazole and that the patent office has neglected the fact that claim 38 is directed to the crystalline sodium salt of benzisoxazole methane sulfonic acid Form II having the characteristics and properties disclosed in the specification. Applicant also argues that the crude crystalline salt of benzisoxazole methane sulfonic acid was not prepared by the same process as applicants' instantly claimed product. This argument is not persuasive as without XRD data in the claim 38, it is impossible to distinguish applicants BOS-Na Form II from any other crystalline sodium salt of benzisoxazole methane sulfonic acid of the prior art, since there is no data in the claims to distinguish applicants' crystalline salt from any other crystalline salt of the compound.

In regards to the 35 USC 102 rejection of claim 38 as being anticipated by US Patent No. 6,677,458, applicant argues that the process disclosed in the '458 patent differs from the process of preparing the instantly claimed product and that there is no evidence that the sodium salt of benzisoxazole methane sulfonic acid prepared by the process of the '458 patent is the crystalline sodium salt of benzisoxazole methane sulfonic acid Form II. This argument is not found persuasive as without XRD data in the claim 38, it is impossible to distinguish applicants BOS-Na Form II from any other

crystalline sodium salt of benzisoxazole methane sulfonic acid of the prior art, since there is no data in the claims to distinguish applicants' crystalline salt from any other crystalline salt of the compound.

In regards to the 35 USC 103 rejection of claims 39-43 as being obvious over US Patent No. 4,172,896, FR 2428033 or US Patent No. 6,677,458, applicant argues that the references do not disclose a crystalline sodium salt of benzisoxazole methane sulfonic acid having the characteristics and properties recited in claimed 39-42 and that just because many solid pharmaceuticals are known to exhibit polymorphism does not necessarily mea that the crystalline sodium salt of benzisoxazole methane sulfonic acid would exhibit polymorphism and it is therefore erroneous for the Office to assert that there is nothing unobvious about the innate nature of a drug in exhibiting polymorphism. This argument is not persuasive as it is known that the sodium salt of benzisoxazole methane sulfonic acid does exhibit polymorphism as can be seen by Form V, see FR 2,428,033. Applicant also argues that if it is difficult to predict how many solid forms of a drug are likely to be found, it would be even more difficult to predict that a particular solid form is likely to be found and the prior art cited does not teach or render obvious a process for preparing applicants' instantly claimed product. Applicant argues that a difference in physical properties not meriting the new polymorph patentable is misplaced an the Office cannot rely on In re Cofer and Ex parte Hartop as the prior art does not suggest the claimed polymorph and does not disclose or render obvious a method for making the claimed polymorph. This argument is not persuasive as the Examiner has established that the prior art recognized that the known compound exists

in different polymorphic forms, see Form V. Furthermore, there is a known or obvious way to manufacture the specific polymorphic form claimed. The prior art does provide motivation to prepare applicants' instantly claimed structure and methods to prepare the claimed crystalline structure. While there may be a large number of parameters to vary in an attempt to find the right parameters for producing the claimed crystalline forms, it is noted that a high level of experimentation in the polymorph art is not necessarily undue experimentation. Applicant has not established why one of ordinary skill in the art would not have been enabled to make the claimed polymorph in view of the prior art since obtaining polymorphs of a known organic pharmaceutically active compound is routing in the art and since organic synthesis of polymorphs is possible. Applicant has only concluded that the preparation of specific polymorphs can be difficult, but has not established sufficiently, or by a preponderance of the evidence, that the preparation of polymorphs does not involve routine experimentation in the polymorph art. It is the state of the prior art that there can be multiple forms of a solid in existence and that these polymorphs are created by varying crystallization processes which began with varying starting materials, utilize varying solvents, varying temperatures and varying reaction times. However, applicant has offered no factual evidence that the general state of the art does not teach or suggest the existence of these forms of the sodium salt of benzisoxazole methane sulfonic acid. There is no factual evidence that the general techniques for preparing polymorphic forms known in the prior art would not accurately provide a particular isolation technique that would produce a specific crystalline form. Therefore, the prior art reference along with the motivation in the art

renders applicants' claims obvious. One would be motivated to prepare the instantly claimed invention since it has long been the practice in the chemical and pharmaceutical arts to produce compound in the form of crystals to secure the product. Further, changing the form, purity or other characteristic of an old product does not render the novel form patentable.

Information Disclosure Statement

The references filed with the remarks of 6/28/2006 is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office. No list of references has been submitted with the provided references. Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claim Objections

Claims 39-43 and 89 are objected to under 37 CFR 1.75 as being a substantial duplicate of claim 38. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP 706.03(k). Each of claims 38-43 and 89 claim the crystalline compound of benzisoxazole methane sufonic acid sodium salt of Form II. While claims 39-43 and 89 recite certain X-ray diffraction, infra red spectrum data or water content for the compound, the data recited is considered properties of the compound and are inseparable from the compound itself. Furthermore, page 20 of the instant specification defines BOS-Na From II as having all of the properties as claimed

in claims 39-43 and 89. Therefore, claims 39-43 and 89 are considered duplicate claims of claim 38. This objection can be overcome by deleting claims 39-43 and 89 and inserting the date from claims 39-43 and 89 into claim 38.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 38-43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. According to Brittain,

> For routing work...one typically compares the powder pattern of the analyte to that of reference materials to establish polymorphic identity. Since every compound produces its own characteristic powder diffraction pattern owing the unique crystallography of its structure, powder X-ray diffraction is clearly the most powerful and fundamental tool for a specification of the polymorphic identity of the analyte. Moreover, the USP general chapter on X-ray diffraction states that the identity is established if the scattering angles of the ten strongest reflections obtained for an analyte agree to within +/- 0.20 degrees with that of the reference material, and if the relative intensities of these reflections do not vary by more than 20 percent. (see Brittain in Polymorphism in Pharmaceutical Solids, p.236).

Claim 38 does not provide any X-ray diffraction pattern data, while claims 39 and 40 contain 5 or less peaks of the X-ray diffraction pattern. Claims 41-43 also contain no X-ray diffraction data. The recitation of 5 or fewer peaks are not specific enough to particularly point out and distinctly claim the product that Applicant regards as his invention. At the very least, the claims should be amended to conform to the general practice in the art according to Brittain, i.e. include at least data for the 10 strongest peaks. However additional data such as the chemical name of the compound (sodium

salt of benzisoxazole methane sulfonic acid), water content and FTIR spectrum data should also be included in order to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In regards to the chemical name of the sodium salt of benzisoxazole methane sulfonic acid form II, BOS-Na Form II, it is noted that while the inventor may be his/her own lexicographer, claims 38-43 do not contain any of the physical data that particularly points out and distinctly claims the product that Applicant regards as his invention, i.e. no claim provides at least the 10 strongest peaks of the X-ray diffraction data. Form II is not a limiting element and does not define a difference in the sodium salt of benzisoxazole methane sulfonic acid. Form II is not a common well recognized term in the art to define anything. While BOS-Na Form II is a term defined by the inventors, the definition is found in the instant specification as the XRD, FTIR, and water content data. It is this data that distinguishes applicants' invention from the prior art and not the term BOS-Na Form II. For example, without XRD data in the claim 38, it is impossible to distinguish applicants BOS-Na Form II from any other crystalline sodium salt of benzisoxazole methane sulfonic acid of the prior art, since there is no data in the claims to distinguish applicants' crystalline salt from any other crystalline salt of the compound.

Claim 89 is rejected under 35 USC 112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims must, under modern claim practice, stand alone to define an invention, Ex parte Fressola, 27 USPQ 2d 1608 (1993). The instant claim 89 does not provide the X-ray powder diffraction pattern of Figure 4 and one must refer

back to the specification to define the invention claimed. It is suggested that the x-ray diffraction pattern be inserted into the claim.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 38-43 and 89 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 2-4 and 10-12 of Patent No. 7,015,330. Although the conflicting claims are not identical, they are not patentably distinct from each other because the conflicting claims are claiming a crystalline sodium salt of benzisoxazole methane sulfonic acid of Form IV with the specific x-ray diffraction data as found in conflicting claim 2. Conflicting claims 2-4 and 10-12 or copending Application No. 10/288135 anticipate applicants' instant claim 38 and are therefore considered as obvious type double patenting as the term Form II does not offer any demarcation of the product from the conflicting claims crystalline product as represented by the compound name since form II is not a notation known in the chemical art representing conventional characteristic in demarcating chemical products. Furthermore, conflicting claims 2-4 and 10-12 render obvious applicants instant claims 39-43 and therefore are considered as obvious type double patenting as the difference between the conflicting claims and the instant claims is that the physical property of the conflicting claim differs. However, one having ordinary skill in the art would find the instant claims prima facie obvious because the instant claims differ from the known product merely by forms and the physical properties innate to the forms. As it was set forth by the court in In re Cofer 148 USPQ 268 and Ex parte Hartop 139 USPQ 525, that a product which are merely different forms of known compounds, notwithstanding

that some desirable results are obtained therefrom, are unpatentable. The instant specification and claims disclose a known compound of the sodium salt of benzisoxazole methane sulfonic acid in Form II, which is ***the same pure substance*** as the prior art, only *having different arrangements and/or different conformations of the molecule*. Mere difference in physical property is well known conventional variation for the same pure substance (see Brittain p. 1-2), i.e. prima facie obvious. For a known compound with defined chemical nature to be patentable for a new form, it must have a patentability basis of an advantage in terms of stability, formulation, solubility, bioavailability, ease of purification, preparation or synthesis, hydroscopicity, recovery or prevention of precipitation, etc.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 38 is rejected under 35 U.S.C. 102(b) as being anticipated by US Patent No. 4,172,896. US Patent No. 4,172,896 discloses solid crystalline compounds of the same chemical structure. Specifically the reference discloses BOS-Na compounds of the formula (V), column 3, which is a crystalline compound, see example 1(column 7, lines 11-14). Please note that one category of patentable invention is a "product". A novel or unobvious chemical product is identified first by its "chemical nature, i.e. elemental content and their rations." It is a well known fact that "many pharmaceutical solids exhibit polymorphism which is frequently defined as the ability of a substance to exist as two or more crystalline phases that have different arrangements and/or conformations of the molecules in the crystal lattice." Thus, *in the strictest sense,*

*polymorphs are different crystalline forms of the **same pure substance** in which the molecules have different arrangements and/or different conformations of the molecules* (see Brittain p. 1-2). The term Form II does not offer any demarcation of the product from the prior art crystalline product as represented by the compound name since form II or other forms in the prior art are not notation known in the chemical art representing conventional characteristic in demarcating chemical products.

Claim 38 is rejected under 35 U.S.C. 102(b) as being anticipated by FR 2428033. FR 2428033 discloses slid crystalline compounds of the same chemical structure. Specifically the reference discloses BOS-Na compounds of the formula V, page 4 which is a crystalline compound, see example 1 (column 8, lines 28-30). Please note that one category of patentable invention is a "product". A novel or unobvious chemical product is identified first by its "chemical nature, i.e. elemental content and their rations." It is a well known fact that "many pharmaceutical solids exhibit polymorphism which is frequently defined as the ability of a substance to exist as two or more crystalline phases that have different arrangements and/or conformations of the molecules in the crystal lattice." Thus, *in the strictest sense, polymorphs are different crystalline forms of the **same pure substance** in which the molecules have different arrangements and/or different conformations of the molecules* (see Brittain p. 1-2). The term Form II does not offer any demarcation of the product from the prior art crystalline product as represented by the compound name since form II or other forms in the prior art are not notation known in the chemical art representing conventional characteristic in demarcating chemical products.

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 38 is rejected under 35 U.S.C. 102(e) as being anticipated by US Patent No. 6,677,458.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

US Patent No. 6,677,458 discloses solid compounds of the same chemical structure. Specifically, the reference discloses BOS-Na on column 4, lines 42-49. Please note that one category of patentable invention is a "product". A novel or unobvious chemical product is identified first by its "chemical nature, i.e. elemental content and their rations." It is a well known fact that "many pharmaceutical solids exhibit polymorphism which is frequently defined as the ability of a substance to exist as two or more crystalline phases that have different arrangements and/or conformations of the molecules in the crystal lattice." Thus, *in the strictest sense, polymorphs are different crystalline forms of the* ***same pure substance*** *in which the molecules have different arrangements and/or different conformations of the molecules* (see Brittain p. 1-2). The term Form II does not offer any demarcation of the product from the prior art

crystalline product as represented by the compound name since form II or other forms in the prior art are not notation known in the chemical art representing conventional characteristic in demarcating chemical products.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 39-43 and 89 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 4, 172,896 and Brittain.

Determination of the scope and content of the prior art

US Patent No. 4,172,896 discloses solid crystalline compounds of the same chemical structure. Specifically the reference discloses BOS-Na compounds of the formula (V), column 3, which is a crystalline compound, see example 1(column 7, lines 11-14).

Brittain teaches us that it is a well known fact that "many pharmaceutical solids exhibit polymorphism which is frequently defined as the ability of a substance to exist as two or more crystalline phases that have different arrangements and/or conformations of the molecules in the crystal lattice." Thus, *in the strictest sense, polymorphs are different crystalline forms of the* ***same pure substance*** *in which the molecules have different arrangements and/or different conformations of the molecules* (see Brittain p. 1-2).

Ascertainment of the difference between the prior art and the claims at issue

The difference between the prior art disclosure and the instant claims is that the physical property of the prior art product was not expressly included. Brittain taught that "in the strictest sense, polymorphs are different crystalline forms of the same pure substance in which the molecules have different arrangements and/or different conformations of the molecules (see Brittain p. 1-2).

Resolving the level of ordinary skill in the pertinent art

One having ordinary skill in the art would find the claims prima facie obvious because the instant claims differ from the known product merely by forms and the

physical properties innate to the forms. As it was recognized in the art that in the pharmaceutical field, many solids exhibit polymorphism which is the innate nature of the particular drug (see US Pharmacopia #23, national formulary #18). There is nothing unobvious about the innate nature of a drug. It is also recognized in the art that the innately existed different "morph" will display different physical properties such as X-ray diffraction patter, melting point etc. (see Brittian p. 178-179, 219). Just because it is "different" does not merit the new form patentability. As it was clearly stated by one having ordinary skill in the art in Brittain (p. 1-2) supra, as well as set forth by the court in In re Cofer 148 USPQ 268 and Ex parte Hartop 139 USPQ 525, that a product which are merely different forms of known compounds, notwithstanding that some desirable results are obtained therefrom, are unpatentable. The instant specification and claims disclosed known compound of the sodium salt of benzisoxazole methane sulfonic acid in Form II, which is ***the same pure substance*** as the prior art, only *having different arrangements and/or different conformations of the molecule*. Mere difference in physical property is well known conventional variation for the same pure substance (see Brittain p. 1-2), i.e. prima facie obvious. For a known compound with defined chemical nature to be patentable for a new form, it must have a patentability basis of an advantage in terms of stability, formulation, solubility, bioavailability, ease of purification, preparation or synthesis, hydroscopicity, recovery or prevention of precipitation etc. (see p. 185).

The instant claims are claiming a product which is the same pure substance as the prior art, and only has different arrangements and/or different conformations of the

molecules without any disclosure of any unexpected properties. The mere differences in the physical properties are well known conventional variations for the same pure substance and are prima facie obvious over the prior art.

Claims 39-43 and 89 are rejected under 35 U.S.C. 103(a) as being unpatentable over FR 2428033 and Brittain.

Determination of the scope and content of the prior art

FR 2428033 discloses slid crystalline compounds of the same chemical structure. Specifically the reference discloses BOS-Na compounds of the formula V, page 4 which is a crystalline compound, see example 1 (column 8, lines 28-30).

Brittain teaches us that it is a well known fact that "many pharmaceutical solids exhibit polymorphism which is frequently defined as the ability of a substance to exist as two or more crystalline phases that have different arrangements and/or conformations of the molecules in the crystal lattice." Thus, *in the strictest sense, polymorphs are different crystalline forms of the* ***same pure substance*** *in which the molecules have different arrangements and/or different conformations of the molecules* (see Brittain p. 1-2).

Ascertainment of the difference between the prior art and the claims at issue

The difference between the prior art disclosure and the instant claims is that the physical property of the prior art product was not expressly included. Brittain taught that "in the strictest sense, polymorphs are different crystalline forms of the same pure substance in which the molecules have different arrangements and/or different conformations of the molecules (see Brittain p. 1-2).

Resolving the level of ordinary skill in the pertinent art

One having ordinary skill in the art would find the claims prima facie obvious because the instant claims differ from the known product merely by forms and the physical properties innate to the forms. As it was recognized in the art that in the pharmaceutical field, many solids exhibit polymorphism which is the innate nature of the particular drug (see US Pharmacopia #23, national formulary #18). There is nothing unobvious about the innate nature of a drug. It is also recognized in the art that the innately existed different "morph" will display different physical properties such as X-ray diffraction patter, melting point etc. (see Brittian p. 178-179, 219). Just because it is "different" does not merit the new form patentability. As it was clearly stated by one having ordinary skill in the art in Brittain (p. 1-2) supra, as well as set forth by the court in In re Cofer 148 USPQ 268 and Ex parte Hartop 139 USPQ 525, that a product which are merely different forms of known compounds, notwithstanding that some desirable results are obtained therefrom, are unpatentable. The instant specification and claims disclosed known compound of the sodium salt of benzisoxazole methane sulfonic acid in Form II, which is ***the same pure substance*** as the prior art, only *having different arrangements and/or different conformations of the molecule*. Mere difference in physical property is well known conventional variation for the same pure substance (see Brittain p. 1-2), i.e. prima facie obvious. For a known compound with defined chemical nature to be patentable for a new form, it must have a patentability basis of an advantage in terms of stability, formulation, solubility, bioavailability, ease of purification,

preparation or synthesis, hydroscopicity, recovery or prevention of precipitation etc. (see p. 185).

The instant claims are claiming a product which is the same pure substance as the prior art, and only has different arrangements and/or different conformations of the molecules without any disclosure of any unexpected properties. The mere differences in the physical properties are well known conventional variations for the same pure substance and are prima facie obvious over the prior art.

Claims 39-43 and 89 are rejected under 35 U.S.C. 103(a) as being obvious over US Patent No. 6,677,458 and Brittain.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing

that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Determination of the scope and content of the prior art

US Patent No. 6,677,458 discloses solid compounds of the same chemical structure. Specifically, the reference discloses BOS-Na on column 4, lines 42-49.

Brittain teaches us that it is a well known fact that "many pharmaceutical solids exhibit polymorphism which is frequently defined as the ability of a substance to exist as two or more crystalline phases that have different arrangements and/or conformations of the molecules in the crystal lattice." Thus, *in the strictest sense, polymorphs are different crystalline forms of the* ***same pure substance*** *in which the molecules have different arrangements and/or different conformations of the molecules* (see Brittain p. 1-2).

Ascertainment of the difference between the prior art and the claims at issue

The difference between the prior art disclosure and the instant claims is that the physical property of the prior art product was not expressly included. Brittain taught that "in the strictest sense, polymorphs are different crystalline forms of the same pure substance in which the molecules have different arrangements and/or different conformations of the molecules (see Brittain p. 1-2).

Resolving the level of ordinary skill in the pertinent art

One having ordinary skill in the art would find the claims prima facie obvious because the instant claims differ from the known product merely by forms and the physical properties innate to the forms. As it was recognized in the art that in the pharmaceutical field, many solids exhibit polymorphism which is the innate nature of the

particular drug (see US Pharmacopia #23, national formulary #18). There is nothing unobvious about the innate nature of a drug. It is also recognized in the art that the innately existed different "morph" will display different physical properties such as X-ray diffraction patter, melting point etc. (see Brittian p. 178-179, 219). Just because it is "different" does not merit the new form patentability. As it was clearly stated by one having ordinary skill in the art in Brittain (p. 1-2) supra, as well as set forth by the court in In re Cofer 148 USPQ 268 and Ex parte Hartop 139 USPQ 525, that a product which are merely different forms of known compounds, notwithstanding that some desirable results are obtained therefrom, are unpatentable. The instant specification and claims disclosed known compound of the sodium salt of benzisoxazole methane sulfonic acid in Form II, which is ***the same pure substance*** as the prior art, only *having different arrangements and/or different conformations of the molecule*. Mere difference in physical property is well known conventional variation for the same pure substance (see Brittain p. 1-2), i.e. prima facie obvious. For a known compound with defined chemical nature to be patentable for a new form, it must have a patentability basis of an advantage in terms of stability, formulation, solubility, bioavailability, ease of purification, preparation or synthesis, hydroscopicity, recovery or prevention of precipitation etc. (see p. 185).

The instant claims are claiming a product which is the same pure substance as the prior art, and only has different arrangements and/or different conformations of the molecules without any disclosure of any unexpected properties. The mere differences

in the physical properties are well known conventional variations for the same pure substance and are prima facie obvious over the prior art.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

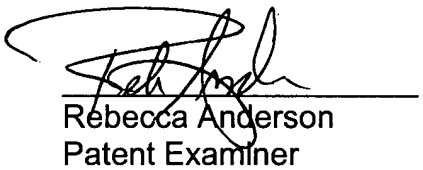
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rebecca L. Anderson whose telephone number is (571) 272-0696. Mrs. Anderson can normally be reached Monday through Friday 5:30AM to 2:00PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mr. Joseph K. McKane, can be reached at (571) 272-0699.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



October 30, 2006

Rebecca Anderson
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